

POLYCYSTIC OVARY SYNDROME AND METABOLIC HEALTH

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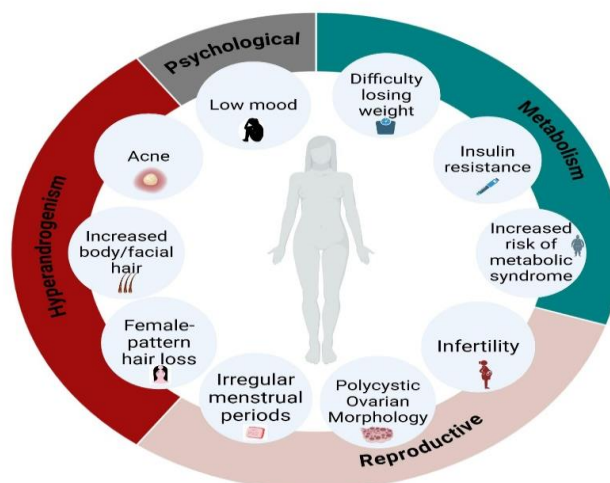
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Abstract

Polycystic ovary syndrome (PCOS) is a complicated genetic condition that impacts around 20% of women. Research indicates that it's a complex condition with multiple genes at play, shaped by both our genes and our surroundings. Diagnosing PCOS depends on reproductive traits and it's split into different types that vary across different races and ethnic backgrounds. Insulin resistance and metabolic issues are key factors in PCOS development; leading to a range of bad metabolic effects that really take a toll on women's health over time. It's interesting to see that women with PCOS often have similar metabolic issues in their family members. We really need to broaden our view of PCOS and seeing it as more than just a fertility issue but also as a metabolic condition. This viewpoint may influence how we plan and handle future care for the condition. The aim of this review is to evaluate and examine the current research backing up the idea that PCOS is both reproductive and a Metabolic issue.

Keywords: PCOS, Metabolic syndrome, metabolites, clinical application and gut microbiota.

Features of Polycystic Ovary Syndrome



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Introduction to Metabolic Syndrome and PCOS

Metabolic syndrome includes things like belly fat, high blood pressure, diabetes and bad cholesterol levels. This emphasizes the vital of heart and hormone health, especially when it comes to insulin intolerance PCOS impacts about 10 to 18 percent of women who can have kids and insulin resistance is a big player in causing it and the related metabolic issues. A lot of women with PCOS possibly have metabolic syndrome, which is notably serious and can lead to heart problems, Hyperglycemia and mental health issues Traditional PCOS management has mostly been about tackling infertility and symptoms tied to it, Illuminating the importance of healthcare pros knowing more about metabolic syndrome Early detection and acting on metabolic syndrome is super important because it's a big health issue. This review will take a deep dive into how metabolic syndrome connects to PCOS, looking at what causes it, what happens because of it, how to spot it, and ways to handle it. This literature really drives home the point that PCOS isn't just a problem with reproduction it's a extensive metabolic issue that can seriously mess with your cardiac physiological function and hormone levels over time. This underscores the need to identify metabolic syndrome early on with regular check-ups and healthy habits like maintaining a healthy weight and getting the right treatments to avoid health problems down the line Given the concern obesity and inactive habits among Indian women, it's crucial to implement prevention strategies that fit the culture at both Healthcare premises and community gatherings to Alleviate the evolving cases of PCOS and metabolic syndromes .

This inspection will explore metabolic syndrome in relation to PCOS and covering its causes, consequences, diagnostic criteria, screening and administration.

Long-term Consequences

Cardiovascular Disease (CVD)

Type II Diabetes

Various forms of Cancer

Sleep Apnea

Psychological disorders

The Pathophysiology of Polycystic Ovary Syndrome: A Comprehensive Treatise

1. Prolegomenon and Diagnostic Taxonomy

Polycystic Ovary Syndrome (PCOS) stands as the preeminent endocrinopathy affecting women of reproductive age, with a global prevalence estimated at approximately 15%. Far from being a mere gynecological concern, PCOS is a multi-systemic disorder characterized by a complex interplay between reproductive failure and metabolic derangement.

The clinical identification of PCOS is governed by several diagnostic frameworks, most notably the Rotterdam Criteria (2003). This consensus requires the presence of at least two of the following three manifestations:

Oligo-ovulation or Anovulation: Irregularity or absence of the menstrual cycle.

Hyperandrogenism: Clinical signs (hirsutism, acne) or biochemical evidence (elevated serum testosterone).

Polycystic Ovarian Morphology (PCOM): The ultrasonographic appearance of numerous small follicles arranged peripherally, often likened to a “string of pearls.”

While the prevalence is uniform across geographies, the phenotypic expression is markedly influenced by ethnicity. Caucasian cohorts frequently exhibit higher body mass indices (BMI), whereas East Asian populations often present with lower BMIs and subtle clinical hyperandrogenism, despite harboring significant internal metabolic disturbances.

I. The Vicious Cycle of Pathogenesis

The pathophysiology of PCOS is not a linear progression but rather a self-perpetuating “vicious cycle” involving the hypothalamus, the pituitary gland, the ovaries, and insulin-sensitive tissues.

A. Neuroendocrine Dysregulation

At the nexus of the disorder is the aberrant pulsation of Gonadotropin-Releasing Hormone (GnRH). In a physiological state, GnRH pulses vary in frequency to regulate the secretion of Luteinizing Hormone (LH) and Follicle-Stimulating Hormone (FSH). In PCOS, the GnRH pulse generator is abnormally rapid, which preferentially stimulates the pituitary to oversecrete LH while suppressing FSH. This imbalance leads to:

Thecal Cell Hyperplasia: Excess LH drives the ovarian theca cells to synthesize high levels of androgens (testosterone).

Follicular Arrest: Insufficient FSH prevents follicles from reaching maturity, leading to the accumulation of small, immature follicles and the characteristic “polycystic” appearance.

B. The Role of Insulin Resistance

Independent of obesity, many women with PCOS exhibit Insulin Resistance (IR). Hyperinsulinemia (excess blood insulin) acts as a co-gonadotropin, directly stimulating ovarian theca cells to produce more androgens. Furthermore, insulin inhibits the hepatic synthesis of Sex Hormone-Binding Globulin (SHBG). As SHBG levels fall, the concentration of bioactive “free” testosterone rises, further exacerbating the androgenic state and reinforcing a cycle of metabolic and reproductive dysfunction.

II. Etiological Drivers: Genetic and Environmental Interplay

The origin of PCOS is multifactorial, emerging from a delicate confluence of genetic susceptibility and environmental triggers.

C. Genetic Architecture

PCOS demonstrates high heritability (approximately 70%). Genome-wide association studies (GWAS) have identified several susceptibility loci, including genes involved in gonadotropin regulation (FSHB, LHCGR) and insulin signaling (INSR). However, these genetic markers account for only a small fraction of the syndrome’s variance, suggesting that environment plays a dominant role in “unlocking” the PCOS phenotype.

D. Environmental and Intrauterine Programming

The “Developmental Origins of Health and Disease” (DOHaD) hypothesis suggests that the intrauterine environment is a critical determinant. Daughters of women with PCOS are exposed to elevated prenatal androgens, which may “program” the fetal hypothalamus and ovaries, predisposed them to PCOS in adulthood.

E. Cellular Stress and Exogenous Toxins

Recent investigations highlight the role of Endoplasmic Reticulum (ER) stress and oxidative stress within the follicular microenvironment. These cellular stressors, often triggered by modern dietary habits—specifically the consumption of Advanced

Glycation End-products (AGEs) found in highly processed or charred foods—disrupt oocyte maturation and exacerbate local inflammation.

III. Epilogue and Future Perspectives

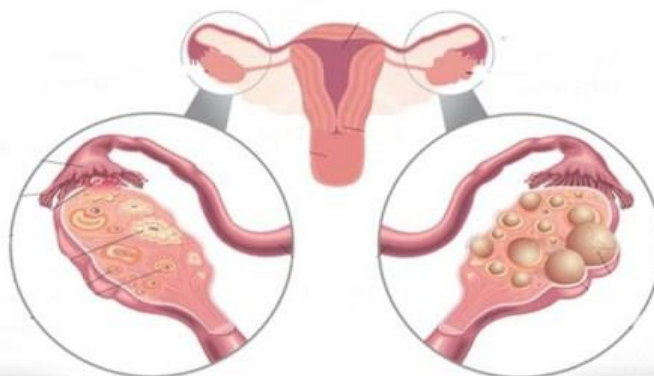
In conclusion, PCOS is a heterogeneous condition where reproductive dysfunction and metabolic disorders intersect. Understanding the syndrome requires moving beyond the ovaries to consider systemic insulin dynamics and cellular health.

Future clinical focus must transcend symptomatic relief (such as the management of acne or cycle regulation) and move toward preconception care and lifelong metabolic vigilance. By addressing the environmental



What is metabolic syndrome in PCOS patients?

- i. Abdominal obesity (waist >88cm).
- ii. Triglycerides (>150mg/dl).
- iii. HDL cholesterol (<50mg/dl).
- iv. B.P >130/ >85 mm of hg.
- v. Glucose (fasting>110mg/dl after 2hrs>140mg/dl).



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Diagnosis

Diagnosed by the at least two specific things from detail but doctors have to rule out other causes for your symptoms first.

- 1 signs of high androgens- like excessive hair growth on your face or body and hair thinning on your head, severe acne. Heightened testosterone levels in your blood.
- 2 Missing or having irregular menstrual period.
- 3 seeing polycystic ovaries on an ultrasound.

Still it's significance noting that not all women with PCOS truly have polycystic ovaries. So, ovarian cysts are not obligatory for PCOS diagnosis.

Blood tests can show elevated androgen steroid levels even if woman who doesn't have obvious excess hair or acne. These tests also help determine if ovulation is occurring regularly for women with normal cycles who might still have PCOS. When doctors are determining for PCOS, they consider genetic inclination -For example, women with a family history of PCOS or type II diabetes have a greater probability of developing the condition themselves. Health professional also take into record a person's life stage. It's rather common for menstrual cycles to be somewhat irregular when someone first starts menstruating, and again as they come closer menopause. Once diagnosed with PCOS, women should go through additional blood tests. These test helps in filter for basic insulin resistance and assess overall cardiac event.

Treatment

PCOS does not have cure but treatment can actually make life improved. Facilitate with fertility, decreased the odds of developing endometrial hyperplasia or endometrial cancer and these treatment helps to stop Prolonged cardiovascular events.

Including a healthy lifestyle with good eating habits and regular exercise is key for all women with PCOS, even if it does not necessarily mean trimming down Combined birth control pills can help keep your period regular and might help clear up your skin or reduce unwanted hair on your face and body. Androgen receptor blockers might also help with unwanted hair or acne When it comes to selecting treatments, it's all about teamwork. We are required to consider what each person truly wants and values Treatments for PCOS-related infertility can range from modifying your lifestyle, taking meds, or even going under the knife to get those eggs to come along IVF and other

fertility help methods might be options too Women with PCOS can often get help to have a baby, but they usually face higher risks during pregnancy that means they need additional check-ups .

Complications

Complications of PCOS can contain:

1. Infertility : Getting pregnant can make more difficult with PCOS but pregnancy Still possible for people dealing with PCOS.
2. Pregnancy difficulty : perhaps you have more chance of getting diabetes during pregnancy, which is known as gestational diabetes. You could have a possibility of dealing with high blood pressure.
3. Mental health concerns : Anxiety, Depression and disorders like eating can occur with PCOS.
4. Metabolic complications : insulin resistant , Type II diabetes (greater chance of high blood sugar).
5. Endometrial cancer : also called uterine cancer, People with PCOS develop a state that induces the uterus lining to become excessively dense.



Etiopathogenesis beyond simple genetics

The etiology of PCOS is best understood as a concordance triggers . While GWAS (Genome wide association studies) have identified susceptibility loci near the DENND1A and FSHR genes, the phenotype rarely manifest without an environmental second hit Most notably , prenatal exposure to high androgen levels may "program " the fetal HPO axis leading to the characteristics increase in GnRH pulse frequency observed in adolescent patient.

THE PATHOGENESIS

the driving force is not a single organ failure but a reciprocal feedback loop

- The intraovarian defect:- in PCOS theca Cells exhibit an intrinsic hyper responsiveness to lutenizing hormone . This over - activity results in the excessive conversion of cholesterol to androstenedione.
- The insulin potentiator:- unlike other tissues that develop insulin resistance the ovary remains paradoxically sensitive to insulin. Hyperinsulinemia acts as a co-gonadotrophic bypassing traditional feedback loops to further drive androgen production while simultaneously down regulating SHBG (Sex hormone binding globulin) . This result in a surge due to the absence of a dominant FSH driven signal .
- Morphology:- microscopically the polycystic appearance is a misnomer. These are not true cysts but are the follicles that has been asserted a cemetery of follicles trapped in the pre antral stage due to the absence of a dominant FSH driven signal .

CLINICAL MANIFESTATION

The clinical presentation is rarely uniform . Patients typically present with a combination of:

1. Dermatological markers:- Refractory cystic acne and hirsutism (tracked via ferriman gallwey scale).
2. Acanthosis Nigricans:- A velvety, hyper pigmented tegument, usually on the nape of the neck or axilla , serving as a visceral marker of severe insulin resistance.
3. Ovulatory Dysfunction:- Chronic oligomenorrhea, which carries the significant risk of endometrial hyperplasia due to lack of cyclic progesterone to offset estrogenic stimulation.

DIAGNOSTICS

- To diagnose PCOS, one must navigate the Rotterdam Criteria, but clinical due diligence requires the active exclusion of:
- NCCAH (Non- classic congenital adrenal hyperplasia) : Often not easily differential than PCOS . A morning 17 - hydroxyprogesterone (17-OHP) level $>2\text{ng/mL}$ is the threshold for further ACTH stimulation testing.
- Androgen secreting neoplasms : Suspected when testosterone levels exceed 200ng/dL or symptoms progress with " virillizing "speed.
- Hypothalamic Amenorrhea: Distinguished by low LH levels and a lack of metabolic markers.

MANAGEMENT

Management is not a one size fits all pill prescription. It requires a systematic and proper approach:

- Metabolic Consolidation:- Metformin remains a essential, not necessarily for weight loss , but for its ability to sensitize peripheral tissues and reduce the insulin burden on the ovaries.
- Hormonal Sequestration:- Combined oral contraceptive (COCPs) are the gold standard for cycle regulations, but clinicians must check for venous thromboembolism (VTE) risk , which is generally higher in PCOS population.
- Infertility Intervention:- while Clomiphene was the historical lead, Letrozole (an aromatase inhibitor) has shown superior live - birth rates by avoiding the anti estrogenic effects on the endometrium seen with older drugs

LONG TERM COMPLICATIONS

The result of untreated PCOS is a metabolic decline .The combination of chronic inflammation and dyslipidemia creates a "pro- thrombotic " state. Studies now show that women with PCOS reach the higher risk for Type2 Diabetes nearly a decade earlier than their peers who are the same weight and height as them . Furthermore, the risk of endometrial adenocarcinoma is elevated three times more due to untreated levels of estrogen.

CONCLUSION

PCOS is dangerous for future metabolic health . Treating the surface level hirsutism or cycle irregularities without addressing the underlying insulin androgen axis is a clinical oversight .

Further direction the transition from a reproductive disorder to a cardiovascular crisis.

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